

amino acid residues of SEQ ID NO:2.>--

Page 24, replace the paragraph beginning on line 6 as follows:

--5. An isolated DNA or a chemically modified nucleic acid derivative thereof, wherein the isolated DNA is a fragmentary sequence of at least 20 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:3.--;

Page 24, replace the paragraph beginning on line 11 as follows:

--6. An isolated DNA or a chemically modified nucleic acid derivative thereof, wherein the isolated DNA is a fragmentary sequence of at least 20 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:4.;

Page 24, replace the paragraph beginning on line 16 as follows:

--7. An isolated RNA or a chemically modified nucleic acid derivative thereof, wherein the isolated RNA is a fragmentary sequence of at least 20 contiguous nucleotides in an RNA which is complementary to the nucleotide sequence of SEQ ID NO:3.--.

Page 44, replace the paragraph beginning on line 16 and bridging pages 44 and 45 as follows:

The C5L2 protein and the fragments thereof are useful for producing an antibody for use in diagnosis and useful for screening pharmaceuticals for treating diseases. Each of the

above-mentioned fragments is a fragmentary peptide having a part of the amino acid sequence of C5L2 protein, specifically a peptide which is a fragmentary sequence of at least 5 contiguous amino acids in the whole C5L2 protein. Like the whole protein, such a fragmentary peptide is useful for the production of an antibody, the screening of a ligand, and the detection of a substance which binds to C5L2 on dendritic cells thereby regulating the functions of dendritic cells so as to treat diseases. For example, a peptide having a sequence of 5 to 8 amino acid residues of an extracellular region or an intracellular region of the receptor is suitable as an antigen used in the preparation of an antibody. Specifically, for example, the fragmentary peptides used in Example 9 of the present specification, namely a fragmentary peptide consisting of the 6th to 32nd amino acid residues of the amino acid sequence of SEQ ID NO:2 and a fragmentary peptide consisting of the 1st to 23rd amino acid residues of the amino acid sequence of SEQ ID NO:2, can be used as antigens. As an example of fragmentary peptides used for screening a ligand, there can be mentioned a peptide having a sequence which is considered to be ligand-binding region(s) of C5L2. More specific examples of such fragmentary peptides include a peptide containing the N-terminal extracellular region (the 1st to 35th amino acid residues of SEQ ID NO:2), the 1st extracellular loop (the 96th to 108th amino

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acid residues of SEQ ID NO:2), the 2nd extracellular loop (the 172nd to 198th amino acid residues of SEQ ID NO:2), or the 3rd extracellular loop (the 681st to 726th amino acid residues of SEQ ID NO:2) of C5L2 protein}--.

Page 48, replace the paragraph beginning on line 5 as follows:

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--The whole length nucleotide sequence of C5L2 obtained by the present inventors is shown in SEQ ID NO:1. A C5L2 clone having a nucleotide sequence which is different from that of SEQ ID NO:1 has also been identified. As a specific example of such clones, a C5L2 clone has been detected, which has a structure in which a further thymine (t) is inserted to the sequence of six contiguous thymines at the site of the 724th to 729th nucleotides of SEQ ID NO:1 (that is, the C5L2 clone has a sequence of seven contiguous thymines at the site which substantially corresponds to the 724th to 729th nucleotides of SEQ ID NO:1). By the use of a nucleic acid probe or primer containing the above-mentioned site of C5L2 of the present invention (i.e., the site consisting of contiguous thymines), it is possible to detect separately a sequence having six contiguous thymines and a sequence having seven contiguous thymines.--.

Page 49, replace the paragraph beginning on line 15 as follows:

--Further, according to the present invention, there

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are also provided an isolated DNA and a derivative thereof, wherein the isolated DNA is a fragmentary sequence of at least 12 contiguous nucleotides in the nucleotide sequence of SEQ ID NO:3 or 4; and an isolated RNA and a derivative thereof, wherein the isolated RNA is a fragmentary sequence of at least 12 contiguous nucleotides in an RNA which is complementary to the nucleotide sequence of SEQ ID NO:3.

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Page 50, replace the paragraph beginning on line 24 and bridging pages 50, 51 and 52 as follows:

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Examples of nucleic acid fragments useful for detecting a C5L2 cDNA or a genomic C5L2 DNA include a fragment comprising a sequence of at least 12 contiguous nucleotides, preferably not less than 16 contiguous nucleotides, more preferably not less than 20 contiguous nucleotides, in the nucleotide sequence of SEQ ID NO:1 or 3, or in a DNA or an RNA which is complementary to the nucleotide sequence of SEQ ID NO:1 or 3. A derivative of the above-mentioned nucleic acid fragments can also be used. The length of the nucleic acid fragment may vary depending on the desired properties of the nucleic acid fragment, such as the specificity and the stability of binding to a nucleic acid to be detected. When PCR (Polymerase Chain Reaction) is conducted using a DNA fragment as a primer, it is preferred to use a DNA fragment having a  $T_m$  (melting temperature of DNA duplex) of 45 °C or more. In the PCR and the like where

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two DNA strands are bound to each other thereby forming a DNA duplex, the  $T_m$  of the DNA duplex can be estimated by calculating the sum of the temperature values assigned to GC pairs and AT pairs in the DNA duplex, wherein 4 °C is assigned to each GC pair and 2 °C is assigned to each AT pair. When a nucleotide sequence to be detected has a high GC content (90 % or more), a DNA fragment which is a sequence of at least 12 contiguous nucleotides can be used. Generally, the GC content of a nucleotide sequence is about 50 %. For detecting such a sequence, a DNA fragment which is a sequence of at least 16 contiguous nucleotides is needed. The binding between a DNA and a nucleic acid derivative is more stable than the binding between two DNAs and, thus, when a nucleic acid derivative is used as a primer, it is possible to detect a desired DNA using a short nucleic acid sequence as compared to the case where a DNA is used as a primer.

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Page 52, replace the paragraph beginning on line 8 and bridging pages 52 and 53 as follows:

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--The examination of the ratio of the expression of the gene of the present invention for the purpose of diagnosis can be conducted by hybridization, primer extension, nuclease protection assay, reverse transcription PCR (RT-PCR) or the like in which a probe or primer designed based on the present invention is used. The probe and primer can be the DNA of SEQ ID NO:4 (i.e.,

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antisense DNA having the sequence complementary to the DNA of SEQ ID NO:3), an RNA complementary to the DNA of SEQ ID NO:3 (i.e., antisense RNA), or a nucleic acid fragment which is a sequence of at least 12 contiguous nucleotides, preferably not less than 16 contiguous nucleotides, more preferably not less than 20 contiguous nucleotides in the above-mentioned DNA or RNA. The antisense DNA or RNA may be a methylated, methyl phosphorylated, deaminated or thiophosphorylated antisense nucleic acid derivative. For example, as shown in Example 4 described below, it is possible to detect the C5L2 mRNA using a fragment of the nucleotide sequence of SEQ ID NO:4 (i.e., the sequence complementary to the DNA of SEQ ID NO:3). --.

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Page 67, replace the paragraph beginning on line 12 and bridging pages 67 and 68 as follows:

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--With respect to the antigen used for producing the antibody of the present invention, there is no particular limitation as long as the antigen has an amino acid sequence of a sufficient length for exhibiting the characteristics of the C5L2 protein. It is preferred that the antigen is a peptide which is a fragmentary sequence of at least 5 contiguous amino acids in the amino acid sequence of SEQ ID NO:2, more advantageously at least 8 contiguous amino acids in the amino acid sequence of SEQ ID NO:2. The antigen peptide is used as such or after cross-linking the peptide with a carrier protein, such as KLH (Keyhole

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Limpet Hemocyanin) or BSA (bovine serum albumin). The antigen peptide (as such or in a form cross-linked with a carrier protein) is inoculated into an animal, wherein, if desired, an adjuvant may be administered together with the antigen peptide. Subsequently, from the animal, an antiserum containing an antibody (polyclonal antibody) recognizing the C5L2 protein can be obtained. The antiserum can be used as such. If desired, the antibody may be purified from the antiserum. Examples of animals into which the antigen peptide is inoculated include a sheep, a cattle, a goat, a rabbit, a mouse, a rat and the like. For the preparation of a polyclonal antibody, the use of a sheep or a cattle is preferred. Specifically, as shown in Example 9 described below, there can be obtained an anti-human C5L2 protein rabbit polyclonal antibody and a solution of an anti-human C5L2 protein rabbit immunoglobulin.

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Page 68, replace the paragraph beginning on line 16 and bridging pages 68 and 69 as follows:

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Further, a monoclonal antibody can be obtained by a conventional method for producing a hybridoma cell. For the production of a monoclonal antibody, it is preferred to use a mouse. As an antigen peptide, there may be used a fusion protein which is obtained by linking GST (glutathione S-transferase) to an antigen peptide which is a fragmentary sequence of at least 5 contiguous amino acids in the amino acid sequence of SEQ ID NO:2,

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preferably at least 8 contiguous amino acids in the amino acid sequence of SEQ ID NO:2. The fusion protein may be either a purified one or a non-purified one. Also, a monoclonal antibody can be obtained by using a gene recombinant antibody which has been expressed in a cell by using an immunoglobulin gene which has been separated by using various methods described in a reference book ("Antibodies a laboratory manual", E. Harlow et al., Cold Spring Harbor Laboratory) and using a gene cloning method.

Page 82, replace the paragraph beginning on line 4 and bridging pages 82 and 83 as follows:

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Examples of primers used for the RT-PCR method include the DNA fragments of the present invention and derivatives thereof, wherein the DNA fragments are fragmentary sequences (each independently being a sequence of at least 12 contiguous nucleotides, preferably not less than 16 contiguous nucleotides, more preferably not less than 20 contiguous nucleotides) in the nucleotide sequences of SEQ ID NOS:3 and 4, respectively. Specific examples of the primers include synthetic primers shown in SEQ ID NOS:9 and 10. The amount of the mRNA encoding C5L2 can be measured by the method described in Example 11 of the present specification. More specifically, the amount of the mRNA encoding C5L2 protein can be measured by a method in which the mRNA encoding the receptor C5L2 in a sample is detected



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by using the primers shown in SEQ ID NOS:9 and 10, whereas the mRNA encoding glyceraldehyde 3-phosphate dehydrogenase (G3PDH) in the same sample as mentioned above is detected by using the primers shown in SEQ ID NOS:11 and 12. The amount of the mRNA encoding C5L2 protein is determined in terms of the ratio of the amount of the mRNA based on the amount of the PCR product for G3PDH (i.e., ratio of the expression of C5L2 based on the expression of G3PDH).-.

Page 83, replace the paragraph beginning on line 3 and bridging pages 83 and 84 as follows:

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-In the present invention, there is no particular limitation with respect to the method for measuring the amount of the C5L2 protein present on the cell surface as long as the amount of the C5L2 protein can be measured specifically. For specifically measuring the amount of the C5L2 protein, it is preferred to use an antibody which specifically binds to C5L2 receptor. Examples of such antibodies include an antibody prepared in Example 9 of the present specification, which is prepared using, as an antigen, a peptide which is a fragmentary sequence of at least 5 contiguous amino acid residues in the amino acid sequence of SEQ ID NO:2. Examples of methods for measuring the amount of the C5L2 protein using the above-mentioned antibody include FACS (employed in Example 11 of the present specification) and immunoprecipitation. With respect to